

REMARKS

Claims 1-15 are pending.

Claims 1-2, 4-5, 8, 9, 11, and 12 stand rejected under 35 USC §103(a) as being allegedly unpatentable over Hoyt (US 2001/0046050) or Hoyt (US 2001/0033374) in view of Kopf-Sill et al (US 6,358,387).

Claims 3, 13, and 14 stand rejected under 35 USC §103(a) as being allegedly unpatentable over Hoyt (US 2001/0046050) or Hoyt (US 2001/0033374) in view of Kopf-Sill et al (US 6,358,387) and further in view of Nordman et al. (US 6,231,739).

Claims 6 and 7 stand rejected under 35 USC §103(a) as being allegedly unpatentable over Hoyt (US 2001/0046050) or Hoyt (US 2001/0033374) in view of Kopf-Sill et al (US 6,358,387) and further in view of Stabile et al. (US 5,854,684).

Claims 10 and 15 stand rejected under 35 USC §103(a) as being allegedly unpatentable over Hoyt (US 2001/0046050) or Hoyt (US 2001/0033374) in view of Kopf-Sill et al (US 6,358,387) and further in view of Modlin et al. (US 2001/0007496).

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned “**VERSION WITH MARKINGS TO SHOW CHANGES MADE.**”

Oath/Declaration:

A new oath/declaration in compliance with 37 CFR 1.67(a) identifying this application by application number 09/915,514 and filing date 07/27/2001 will be submitted shortly.

Changes in the Abstract:

The Abstract has been replaced in accordance with the Examiner's suggestion in order to better conform to US patent practice. All instances of reference numerals to figures are removed. "Fig. 1" at line 11 has been deleted.

Changes in the Specification:

The specification has been amended for the purpose of improving the readability of the application and are of a clerical, typographical or grammatical nature. No new matter has been added.

Changes in the Claims:

Claims 1, 2, and 3 have been amended to overcome the Office Action's objections over insufficient antecedent basis.

Claims 1-11 and 13-14 have been amended or added in this application to further particularly point out and distinctly claim subject matter regarded as the invention. The amendments are supported in the specification at page 5, line 16- page 6, lines 20. No new matter has been added.

Rejection under 35 USC §103(a) – claims 1-2, 4-5, 8, 9, 11, and 12

Claims 1-2, 4-5, 8, 9, 11, and 12 stand rejected under 35 USC §103(a) as being allegedly unpatentable over Hoyt (US 2001/0046050) or Hoyt (US 2001/0033374) in view of Kopf-Sill et al (US 6,358,387). This rejection is respectfully traversed.

Under MPEP §706.02(j), in order to establish a prima facie case of obviousness required for a §103 rejection, three basic criteria must be met: (1) there must be some suggestion or motivation either in the references or knowledge generally available to modify the reference or combine reference teachings (MPEP §2143.01), (2) a reasonable expectation of success (MPEP §2143.02), and (3) the prior art must teach or suggest all the claim limitations (MPEP §2143.03). See In re Royka, 490 F. 2d 981, 180 USPQ 580 (CCPA 1974).

Hoyt teaches an apparatus that provides a beam of light which is split into a plurality of output beams by a diffractive beam splitter, which beams in polarization state illuminate samples at plate, yielding fluorescent light.

Kopf-Sill teaches a structure of microchannels defining a plane. The excitation beam is focused on this plane as a **large aspect ratio elliptical illumination beam**. See col. 16, lines 55-57 and Fig. 3. In particular, source and optical elements are positioned such that the elliptical excitation beam impinges on substrate at a **non-normal angle of incidence** ϕ . Kopf-Sill further teaches that the angle of incidence ϕ should be approximately 45° relative to the plane defined by the substrate, although other non-normal angles of incidence may be used. See col. 16, lines 60-66.

Applicant requests reconsideration of claims 1-2, 4-5, 8, 9, 11, and 12 rejection because the proposed combination of Hoyt and Kopf-Sill does not teach or suggest the presently claimed invention. In particular, the presently claimed invention claims the limitation of guiding a polarized light into N parallel microchannels “so as to obtain N fluorescent sections.” See Claim 1. The above limitation indicates that light propagates along the axis of the microchannels. The angle of incidence of the polarized light relative

to the plane defined by the microchannels is approximately 90° . See Figs. 1, 2, and 3. In contrast, Hoyt and Kopf-Sill teach only a non-normal angle of incidence (from about 30° to 60°).

Furthermore, the presently claimed invention claims constituents to be analyzed that are illuminated with polarized light propagating along the axis of the microchannels so as to obtain N fluorescent sections. See claim 1. In contrast, Hoyt and Kopf-Sill suggest substances in the microfluidic channels that are always excited by an elliptical beam and not by light propagating along the axis of the microchannels. See col. 17, lines 13-15.

Applicant therefore submits that the rejection based Hoyt and Kopf-Sill is improper and should be withdrawn. Thus, Applicant submits that claims 1-15 recite novel subject matter which distinguishes over any possible combination of Hoyt and Kopf-Sill.

Rejection under 35 USC §103(a) – claims 3, 13, and 14

Claims 3, 13, and 14 stand rejected under 35 USC §103(a) as being allegedly unpatentable over Hoyt (US 2001/0046050) or Hoyt (US 2001/0033374) in view of Kopf-Sill et al (US 6,358,387) and further in view of Nordman et al. (US 6,231,739). This rejection is respectfully traversed.

These rejections are respectfully traversed for at least the reason that each of the rejected claims ultimately depend on an above-discussed base claim. The arguments set forth above regarding the base claims are equally applicable here. The base claims being allowable, the dependent claims must also be allowable.

Rejection under 35 USC §103(a) – claims 6 and 7

Claims 6 and 7 stand rejected under 35 USC §103(a) as being allegedly unpatentable over Hoyt (US 2001/0046050) or Hoyt (US 2001/0033374) in view of Kopf-Sill et al (US 6,358,387) and further in view of Stabile et al. (US 5,854,684). This rejection is respectfully traversed.

These rejections are respectfully traversed for at least the reason that each of the rejected claims ultimately depend on an above-discussed base claim. The arguments set forth above regarding the base claims are equally applicable here. The base claims being allowable, the dependent claims must also be allowable.

Rejection under 35 USC §103(a) – claims 10 and 15

Claims 10 and 15 stand rejected under 35 USC §103(a) as being allegedly unpatentable over Hoyt (US 2001/0046050) or Hoyt (US 2001/0033374) in view of Kopf-Sill et al (US 6,358,387) and further in view of Modlin et al. (US 2001/0007496). This rejection is respectfully traversed.

These rejections are respectfully traversed for at least the reason that each of the rejected claims ultimately depend on an above-discussed base claim. The arguments set forth above regarding the base claims are equally applicable here. The base claims being allowable, the dependent claims must also be allowable.

Conclusion

For all of the above reasons, applicants submit that the amended claims are now in proper form, and that the amended claims all define patentable subject matter over the prior art. Therefore, Applicants submit that this application is now in condition for allowance.

Request for allowance

It is believed that this Amendment places the above-identified patent application into condition for allowance. Early favorable consideration of this Amendment is earnestly solicited. If, in the opinion of the Examiner, an interview would expedite the prosecution of this application, the Examiner is invited to call the undersigned attorney at the number indicated below.

Respectfully submitted,
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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Abstract:

The abstract has been amended as follows:

-- The invention relates to a polarized light fluorescence imaging device comprising a structure of parallel microchannels [(4)] for containing the constituents to be analyzed. A coupling device [(2, 5)] enables polarized light to be guided into the microchannels.

The invention is applied to the analysis of [labelled] labeled nucleic acid sequences.

[Fig. 1.]--

In the Specification:

The paragraph beginning at page 1, line 20 has been replaced with the following rewritten paragraph:

-- More recently, polarized fluorescence was used for analysis of labelled nucleic acid sequences. So, let us cite the article, "Fluorescence Polarization in Homogenous [Nuclei] Nucleic Acid Analysis" by Chen, Levine and Kwok, Genome Research, 09/98, and the article, "A homogeneous method for genotyping with fluorescence polarization", by Neil J. Gibson, Helen L. Gillard, David Whitcombe, Richard M. Ferrie, Clive R. Newton and Stephen Little, Clinical Chemistry 43: 8, 1336-1341.--

The paragraph beginning at page 2, line 1 has been replaced with the following rewritten paragraph:

-- "Fluorescence Anisotropy: Rapid, Quantitative Assay for [Protein-DANA] Protein-DNA and Protein-Protein Interaction" by Tomasz Heyduk, Yuexing Ma, Hong Tang and Richard H. Ebricht, Methods in Enzymology, Vol. 274, and --

The paragraph beginning at page 2, line 18 has been replaced with the following rewritten paragraph:

-- A great number of devices for implementing fluorescence polarization measurements are known from the prior art. For instance, spectrophotometers [provides] provided with polarization accessories may be mentioned. The investigated spectra are then spectra from monochromators, in front of which are placed polarization filters. White light is vertically polarized before reaching the sample and the sample's fluorescence is alternately analyzed with vertical then horizontal polarization. The degree of polarization is given by the formula below:--

The paragraph beginning at page 3, line 5 has been replaced with the following rewritten paragraph:

-- These spectra have the advantage of allowing the whole spectral range to be explored, both in emission and in excitation. However, they lack sensitivity as the monochromators [are] have very selective films [which have] with a relatively high attenuation.--

The paragraph beginning at page 3, line 16 has been replaced with the following rewritten paragraph:

-- There are also investigation benches with two simultaneous channels. Now, n measurement points may be scanned, but this requires mechanical motion and a synchronization device which make implementation delicate [of] for these benches in an industrial environment.--

The paragraph beginning at page 7, line 3 has been replaced with the following rewritten paragraph:

-- With optics 10 and polarizing filters 6 and 7, the N parallel microchannels may be imaged on a CCD (Charge Coupled Device) camera 8. As a non-limiting example, polarizing filters 6 and 7 are mounted on a filter wheel 9. The fluorescence light F from the N microchannels is then detected. The imaging of the N microchannels is performed, first of all according to a first direction of polarization then according to the direction perpendicular to the first direction of polarization. Two channel intensities $I_{//}$ and I_{\perp} are thereby obtained, channel by channel. The resulting polarization is given by:--

The paragraph beginning at page 7, line 21 has been replaced with the following rewritten paragraph:

-- According to this second example, two different tracers are imaged. For example, they may be R110 and TAMRA as mentioned earlier. The device comprises an objective lens 10, a CCD camera 8 and [4] four polarizing filters 11, 12, 13 and 14 mounted on a filter wheel 15. Filters 11 and 12 filter the vertical polarization and the horizontal polarization of the fluorescent light from a first tracer, respectively and filters 13 and 14 filter the vertical polarization and the horizontal polarization of the fluorescent light from

the second tracer, respectively. The respective intensities $I_{//R110}$, $I_{\perp LR110}$, $I_{//TAMRA}$ and $I_{\perp TAMRA}$ are then successively measured by camera 8. For this purpose, the filter wheel 15 is switched with both excitation laser beams (not shown in the figure) synchronously, which successively illuminate the microchannels.--

In the claims:

Claims 1-11 and 13-14 have been amended as follows:

1. (Once Amended) A fluorescence image device comprising:

first means for containing constituents to be analyzed[,];

second means for illuminating with polarized light the constituents to be analyzed; and

third means for reading out a fluorescence light emitted by the constituents under the action of the polarized light,

[characterized in that the] said first means [consist of] having a structure of N parallel [microchannel structure (4) and in that the] microchannels, N being an integer,

said second means [comprise] having at least one coupling device [(2, 5)] for guiding said polarized light into [the] said N parallel microchannels so as to obtain N fluorescent sections.

2. (Once Amended) The device according to claim 1, characterized in that [the] said N parallel microchannels are etched in a glass or high optical quality plastic or silicon support chip.

3. (Once Amended) The device according to claim 1, characterized in that [the] said N parallel microchannels are flexible capillaries.
4. (Once Amended) The device according to claim 1, characterized in that the coupling device comprises a diffraction grating [(5)].
5. (Once Amended) The device according to claim 1, characterized in that the coupling device comprises a cylindrical lens [(2)].
6. (Once Amended) The device according to claim 1, characterized in that the second means comprise a laser or a microlaser for illuminating the whole of the microchannel structure [(4)] and in that the third means comprise a first polarizing filter [(6, 11, 13)] for filtering, firstly, a first component of the polarized fluorescence light according to a first direction and a second polarizing filter [(7, 12, 14)] for filtering, secondly, a second component of the polarized fluorescence light according to a direction perpendicular to the first direction.
7. (Once Amended) The device according to claim 6, characterized in that it comprises a filter wheel [(9, 15)] for switching the first filter [(6, 11, 13)] and the second filter [(7, 12, 14)].
8. (Once Amended) The device according to claim 1, characterized in that the second means comprise a laser or microlaser for illuminating the whole of the microchannel

structure [(4)] and in that the third means comprise a birefringent crystal [(16, 1-7)] for separating the fluorescence light emitted according to two components polarized perpendicularly to each other.

9. (Once Amended) The device according to claim 6, characterized in that the laser or microlaser emits at a first wavelength $[(\lambda_1)]$ substantially between 488 nm and 514 nm or at a second wavelength $[(\lambda_2)]$ substantially between 550 nm and 580 nm.

10. (Once Amended) The device according to claim 1, characterized in that the second means comprise a first laser or microlaser for illuminating a first area of [the microchannel structure (4)] said structure of N parallel microchannels and a second microlaser for simultaneously illuminating a second area of [the microchannel structure (4)] said structure of N parallel microchannels and in that the third means comprise a birefringent crystal [(16, 17)] for separating the fluorescence light emitted according to two components polarized perpendicularly to each other.

11. (Once Amended) The device according to claim 10, characterized in that the first laser or microlaser emits at a first wavelength $[(X_1)]$ substantially between 488 nm and 514 nm and the second microlaser emits at a second wavelength $[(X_2)]$ substantially between 530 nm and 550 nm.

12. (Not Amended) The device according to claim 8, characterized in that the birefringent crystal is LiNbO₃ crystal or a calcite crystal.

13. (Once Amended) The device according to claim 3, characterized in that the coupling device comprises a diffraction grating [(5)].

14. (Once Amended) The device according to claim 3, characterized in that the coupling device comprises a cylindrical lens [(2)].

15. (Not Amended) The device according to claim 10, characterized in that the birefringence crystal is a LiNbO₃ crystal or a calcite crystal.